

IN THE CLAIMS

Please amend claims 2-6 as shown below. Please cancel claims 7-9, 11, and 23-26, without prejudice. Please add new claims 30-44 as shown below. The following listing of claims replaces all prior listings.

1. (Canceled).
2. (Currently amended) The ~~compound~~ article of manufacture of claim 23 30, wherein E₁, E₃, and E₄ are -O, and E₂ is -NH.
3. (Currently amended) The ~~compound~~ article of manufacture of claim 23 30, wherein R₁ and R₂ are -H, alkyl, or substituted alkyl, and R₃ is hydroxy or alkoxy.
4. (Currently amended) The ~~compound~~ article of manufacture of claim 23 30, wherein R₁ is substituted alkyl.
5. (Currently amended) The ~~compound~~ article of manufacture of claim 4, wherein the substituted alkyl is a halogenated alkyl.
6. (Currently amended) The ~~compound~~ article of manufacture of claim 5, wherein the halogenated alkyl is a chlorinated alkyl.
- 7-14. (Canceled)
15. (Withdrawn) The method of claim 27, wherein the mammalian cell is human.
16. (Withdrawn) The method of claim 27, wherein the disorder is characterized by the formation of neoplasms.
17. (Withdrawn) The method of claim 16, wherein the neoplasms are selected from mammary, small-cell lung, non-small-cell lung, colorectal, leukemia, melanoma, pancreatic adenocarcinoma, central nervous system (CNS), ovarian, prostate, sarcoma of soft tissue or bone, head and neck, gastric which includes thyroid and non-Hodgkin's disease, stomach,

myeloma, bladder, renal, neuroendocrine which includes thyroid and non-Hodgkin's disease and Hodgkin's disease neoplasms.

18. (Withdrawn) The method of claim 17, wherein the neoplasms are colorectal neoplasms.

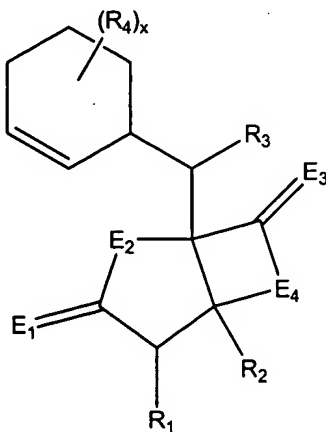
19. (Withdrawn) A method for inhibiting proliferation of mammalian cells, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of claim 23.

20. (Withdrawn) The method of claim 19, wherein the mammalian cells are human.

21. (Withdrawn) The method of claim 20, wherein the cells are selected from mammary, small-cell lung, non-small-cell lung, colorectal, leukemia, melanoma, pancreatic adenocarcinoma, central nervous system (CNS), ovarian, prostate, sarcoma of soft tissue or bone, head and neck, gastric, stomach, myeloma, bladder, renal, and neuroendocrine cells.

22-26. (Canceled)

27. (Withdrawn) A method for treating a mammalian cell proliferative disorder, comprising administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



I

wherein:

R₁ to R₃ are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfuryl,

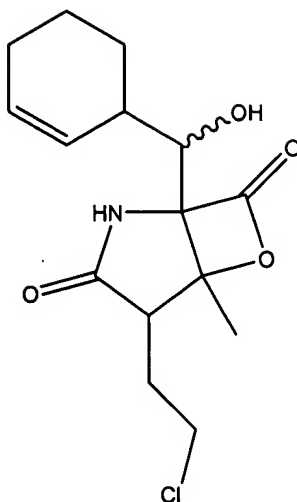
each R₄ is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

E₁ to E₄ are each independently -O, -NR₅, or -S, wherein R₅ is -H or C₁-C₆ alkyl, and

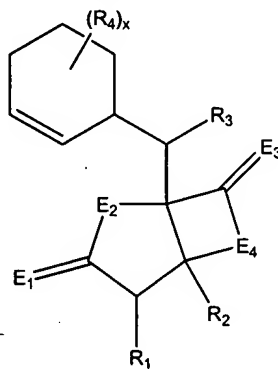
x is 0 to 8'

thereby treating a mammalian cell proliferative disorder.

28. (Withdrawn) The method of claim 27, wherein the compound has the structure:



29. (Withdrawn) A method for producing a compound having the ability to inhibit the proliferation of hyperproliferative mammalian cells, wherein said compound has structure (I):



I

wherein:

R_1 to R_3 are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfuryl,

each R_4 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

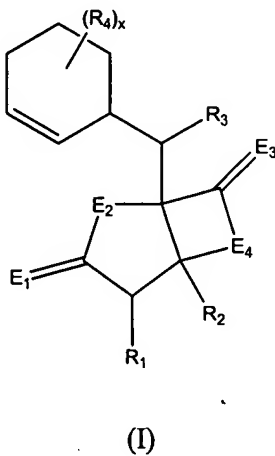
E_1 to E_4 are each independently $-O$, $-NR_5$, or $-S$, wherein R_5 is $-H$ or C_1 - C_6 alkyl, and

x is 0 to 8,

the method comprising:

- a) cultivating a culture of a *Salinospora* sp. strain CNB392 or CNB476;
- b) isolating from the culture at least one compound of structure (I).

30. (New) An article of manufacture comprising packaging material and a pharmaceutical composition contained within said packaging material, wherein said packaging material comprises a label which indicates that said pharmaceutical composition can be used for treatment of cell proliferative disorders and wherein said pharmaceutical composition comprises at least one compound having the structure (I):



wherein:

R_1 to R_3 are each independently $-H$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted

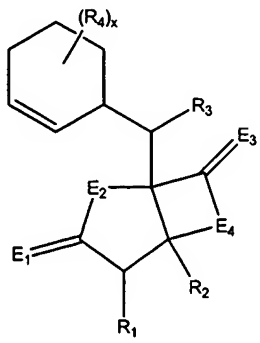
heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfuryl,

each R_4 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

E_1 to E_4 are each independently -O, -NR₅, or -S, wherein R_5 is -H or C₁-C₆ alkyl, and

x is 0 to 8.

31. (New) A pharmaceutical composition useful for inhibiting proliferation of hyperproliferative mammalian cells, comprising an effective amount of a compound having the structure (I) and a pharmaceutically acceptable carrier:



I

wherein:

R_1 to R_3 are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted

heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy,
thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl,
-C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfuryl,

each R₄ is independently alkyl, substituted alkyl, alkenyl,
substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl,
cycloalkyl, substituted cycloalkyl,

E₁ to E₄ are each independently -O, -NR₅, or -S, wherein R₅ is -H
or C₁-C₆ alkyl, and

x is 0 to 8,

and further comprising at least one additional anti-neoplastic agent.

32. (New) The composition of claim 31, wherein E₁, E₃, and E₄ are -O, and E₂ is -NH.

33. (New) The composition of claim 31, wherein R₁ and R₂ are -H, alkyl, or substituted alkyl, and R₃ is hydroxy or alkoxy.

34. (New) The composition of claim 31, wherein R₁ is substituted alkyl.

35. (New) The composition of claim 34, wherein the substituted alkyl is a halogenated alkyl.

36. (New) The composition of claim 35, wherein the halogenated alkyl is a chlorinated alkyl.

37. (New) The composition of claim 31, wherein the anti-neoplastic agent comprises an antimetabolite, an alkylating agent, a plant alkaloid, an antibiotic, a hormone, or an enzyme.

38. (New) The composition of claim 37, wherein the antimetabolite is selected from a group consisting of methotrexate, 5-fluorouracil, 6-mercaptopurine, cytosine arabinoside, hydroxyurea, and 2-chlorodeoxyadenosine.

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39. (New) The composition of claim 37, wherein the alkylating agent is selected from a group consisting of cyclophosphamide, melphalan, busulfan, paraplatin, chlorambucil, and nitrogen mustard.

40. (New) The composition of claim 37, wherein the plant alkaloid is selected from a group consisting of vincristine, vinblastine, taxol, and etoposide.

41. (New) The composition of claim 37, wherein the antibiotic is selected from a group consisting of doxorubicin (adriamycin), daunorubicin, mitomycin c, and bleomycin.

42. (New) The composition of claim 37, wherein the hormone is selected from a group consisting of calusterone, diomostavolone, propionate, epitiostanol, mepitiothane, testolactone, tamoxifen, polyestradiol phosphate, megesterol acetate, flutamide, nilutamide, and trilotane.

43. (New) The composition of claim 37, wherein the enzyme is selected from a group consisting of L-asparaginase derivatives and aminoacridine derivatives.

44. (New) The composition of claim 43, wherein the aminoacridine derivative is amsacrine.